CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
75-366

CORRESPONDENCE

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

April 5, 1999

Florence Fang, Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
7500 Standish Place
Metro Park North II
Rockville, MD 20857

NDA ORIG AMENDMENT
N/A x 1

-MINOR AMENDMENT-

Reference: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Dr. Fang :

Reference is made to your letter dated March 8, 1999 for our Abbreviated New Drug Application for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA 75-366. The following are our responses to the deficiencies noted in your letter:

1. **We have issued another deficiency letter to the DMF holder for the drug substance under Please be aware that a satisfactory review of the drug Master File is essential for the approval of your new drug application.**

   We have recently been advised by hat the DMF deficiencies have been addressed and submitted to the FDA in an amendment dated March 31, 1999 .

2. **Please note that our office policy requires routine in-process blend testing for every production batch post-approval.**

   We commit to performing routine in- process blend testing for every production batch post-approval. Included are the **Quality Control In- Process Specifications & Report Form** for each strength of Sotalol Hydrochloride Tablets *(Attachment 1)*.

3. **It is recommended that an methodology be employed for potency determination since it is more accurate and specific. Please revise your product specifications for Release and for Shelf-life accordingly (including limit, if necessary).**

   Potency determination for the finished product release and stability testing are in fact

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APR 0 6 1999
GENERIC DRUGS

4-7-99

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

August 13, 1999

Douglas L. Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

-MINOR AMENDMENT-

Re: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Mr. Sporn:

In response to your letter dated July 26, 1999 granting tentative approval for our original Abbreviated New Drug Application for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA # 75-366, we are submitting a minor amendment at least 60 days prior to the expiration of the orphan drug exclusivity, October 30, 1999, for Betapace®.

All chemistry and manufacturing controls information remain the same as currently approved with the exception of the following:

- Updated Eon-Labs in-house effective date 6/24/99 **(Attachment 1).** The method was changed to increase the n time from 6 times to 12 times the retention time of the sotalol peak to ensure that all of the related compounds are eluted.

  This method was amended as per a recent commitment made in response to a pre-approval inspection for the subject product at Eon Labs Manufacturing Inc., Laurelton, NY. No other changes to our application have been made.

If there are any further comments or questions regarding this submission, please feel free to contact me at (718) 276-8607, extension 423.

Sincerely,
Eon Labs Manufacturing, Inc.

Patricia Kaufold
Patricia Kaufold
Manager, Regulatory Affairs

MAR 8 1999

38. Chemistry Comments to be Provided to the Applicant

ANDA: #75-366 **APPLICANT:** Eon Labs Manufacturing, Inc.

DRUG PRODUCT: Sotalol Hydrochloride Tablets 80 mg, 120 mg, 160 mg and 240 mg

The deficiencies presented below represent MINOR deficiencies

Chemistry Deficiencies:

1. We have issued another deficiency letter to the DMF holder for the drug substance under DMF Please be aware that a satisfactory review of the Drug Master File is essential for the approval of your new drug application.

2. Please note that our office policy requires routine in-process blend testing for every production batch post-approval.

3. It is recommended that an methodology be employed for potency determination since it is more accurate and specific. Please revise your product specifications for Release and for Shelf-life accordingly (including limit, if necessary).

Sincerely yours,

Florence Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

January 22, 1999

Florence Fang, Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
7500 Standish Place
Metro Park North II
Rockville, MD 20857

-MINOR AMENDMENT-

Reference: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Dr. Fang :

Reference is made to your letter dated December 31, 1998 for our Abbreviated New Drug Application for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA 75-366. The following are our responses to the deficiencies noted in your letter:

1. **DMF .or the drug substance Sotalol Hydrochloride was reviewed and found inadequate. A letter listing the deficiencies has been issued to the holder Please be aware that a satisfactory review of the Drug Master file is essential for the approval of your new drug application.**

   We have recently been advised by .hat the DMF deficiencies have been addressed and submitted to the FDA in an amendment dated January 18, 1999

2.

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JAN 25 1999

batches, including in-process blend testing.

3.

4.

Labeling Deficiencies:

1. CONTAINER 80 mg (100s) 120 mg, 160 mg, 240 (100s and 500s)

   a. **Correct the hyphenation of the word "temperature".**

   b. **Increase the blank vertical space between the left panel and the main panel.**

   c. **The statement "Dispense contents.. "appears to run into the text on the main panel.**

d. 160 mg - 500s only - Delete the hyphen in the word "accompanying".

2. INSERT

a. GENERAL COMMENTS

i. There is no need to capitalize "sotalol" unless required by sentence structure.

ii. Be consistent with the prominence of the subsection heading throughout the text.

iii. Replace the hyphen with the word "to" when expressing a range throughout the text.

b. DESCRIPTION

i. Delete the word "tablets" in the first sentence.

ii. "anhydrous lactose" rather than "lactose anhydrous".

iii. "pregelatinized" (spelling).

c. CLINICAL PHARMACOLOGY

i. Delete "hydrochloride" and hydrochloride tablets" throughout this section wherever it occurs except in the following places:

A). Mechanism of Actions - second sentence

B). Hemodynamics - first sentence

C). Clinical Actions

1). Second occurrence in the paragraph beginning "In a double-blind . . ."

2). First occurrence in the paragraph beginning "In a large double-blind . . ."

D). Pharmacokinetics - second occurrence

ii. Delete "tablets" in the first sentence of the "Hemodynamics" subsection.

b. INDICATIONS AND USAGE

i. Revise the section title as seen above.

ii. Delete "hydrochloride and hydrochloride tablets" throughout this section wherever it occurs except in the first sentence.

e. CONTRAINDICATIONS

Sotalol hydrochloride is contraindicated . . .

a. WARNINGS

i. Delete "hydrochloride" throughout this section wherever it occurs except in the following places:

A). Second occurrence in the paragraph beginning " The applicability of . . ."

B). Abrupt withdrawal - the second occurrence

ii Recent Acute MI, second sentence - "from" (spelling)

iii. Non-Allergic Bronchospasm - Increase the spacing between the bolded capitalized words.

g. PRECAUTIONS

i. Delete "hydrochloride" throughout this section.

ii. Decrease the prominence of the subsection title "DRUG INTERACTIONS".

iii. "Pregnancy: Pregnancy Category B:" should be the subsection title.

iv. Pediatric Use - "pediatric patients" rather than "children"

b. ADVERSE REACTIONS

i. Delete "hydrochloride" throughout this section.

ii. Table - "prarrhythmia" (lower case "p")

iii. Potential Adverse Effects, first paragraph last sentence

A). "photosensitivity" (delete the hyphen)

B). "pruritus" (spelling)

i. OVERDOSAGE

Symptoms and Treatment of Overdosage

i. First sentence - "hypoglycemia" (delete hyphen)

ii. Fourth sentence - "concentrations" (plural)

iii. Delete the second occurrence of "Bradycardia or Cardiac Asystole".

a. DOSAGE AND ADMINISTRATION

i. Delete "hydrochloride" in the second sentence and in the sentence immediately before the "Dosage and Renal Impairment" subsection and all others which occur from this subsection through to the "HOW SUPPLIED" section.

ii. Dosage in Renal Impairment

A). Decrease the prominence of the heading.

B). Delete the last paragraph of this subsection and replace it with the following text:

. . . tablet above).

Pharmacokinetic finds in patients requiring chronic hemodialysis is limited to six patients in two studies. In these patients, terminal elimination half life is prolonged to 40 hours in the interdialysis period and approaches 7 hours during dialysis. Ti is estimated that 20% to 40% of sotalol is removed during dialysis and that a slight rebound of plasma concentration is noted post dialysis. Extreme caution must be taken in renal failure requiring

hemodialysis, usual parameter of safety and efficacy (heart rate , QT interval and control of arrhythmia) must be closely monitored.

k. HOW SUPPLIED

xi. "tablets" (lower case "t")

xii. We encourage the use of the NDC number in this section.

xiii. Insert a blank space between the word "closure"and "(as required)".

xiv. We encourage you to relocate the symbol "Rx only" to under the Title of the insert.

Final Printed labels and labeling have been revised to include your observations and are being submitted *(Attachment 1)*. To facilitate review of this submission, included is a side by side comparison of the current insert and the last submission with all differences annotated and explained *(Attachment 2)*.

Please note that we do not include NDC numbers on our insert. This is due to the fact that the same insert is used by our private customer label distributors and therefore, it would be inappropriate to include NDC numbers.

In response to the comments received from the Division of Bioequivalence , for dissolution testing, we have revised the dissolution testing parameters in our stability and quality control programs to be in conformance with the recommended specification. The following documents now include the new specification and are being submitted *(Attachment 3)*.

- **Quality Control Finished Tablet Specification & Report Form**
- **Post Approval Stability Commitment**
- **Product Monograph**

If there are any comments or questions regarding this submission, please contact me at (718) 276-8607, extension 446.

Sincerely,
Eon Labs Manufacturing, Inc.

Amal Shaker
Sr. Regulatory Affairs Associate

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-365 APPLICANT: Eon Labs Manufacturing Inc.

DRUG PRODUCT: Sotalol Tablets, 80 mg, 120 mg, 160 mg and 240 mg

The Division of Bioequivalence has completed its review and has no further questions at this time.

The following dissolution testing will need to be incorporated into your stability and quality control programs:

> The dissolution testing should be conducted in 900 mL of water, at 37 ^{0}C using USP Apparatus (II) at 50 rpm. The test product should meet the following specifications:
>
> Not less than amount of the drug in the dosage form is dissolved in 30 minutes.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

DEC 31 1998

38. Chemistry Comments to be Provided to the Applicant

ANDA: #75-366 APPLICANT: Eon Labs Manufacturing, Inc.

DRUG PRODUCT: Sotalol Hydrochloride Tablets 80 mg, 120 mg, 160 mg and 240 mg

The deficiencies presented below represent MINOR deficiencies

A. Chemistry Deficiencies:

1. DMF for the drug substance Sotalol Hydrochloride was reviewed and found inadequate. A letter listing the deficiencies has been issued to the holder, Irotec. Please be aware that a satisfactory review of the Drug Master File is essential for the approval of your new drug application.

2. Since the active ingredient is less than of the tablet, we recommend in-process blend uniformity analysis for all strengths of the drug product. The acceptance criteria of of label claim (mean of individual test results) with a relative standard deviation (RSD) should be used for blend uniformity analysis. Please revise your blank batch records accordingly.

3. We note that you have performed all the validation studies on the method for potency determination for the finished drug product. Do you consider using method for routine potency testing of the active ingredient?

4. For future stability studies, please be advised that the long-term stability test storage conditions may be at 25° to 30°C with ambient humidity or 25°C ± 2°C/60% RH ± 5%.

Sincerely yours,

Florence Fang
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-365 APPLICANT: Eon Labs Manufacturing Inc.

DRUG PRODUCT: Sotalol Tablets, 80 mg, 120 mg, 160 mg and 240 mg

The Division of Bioequivalence has completed its review and has no further questions at this time.

The following dissolution testing will need to be incorporated into your stability and quality control programs:

> The dissolution testing should be conducted in 900 mL of water, at 37 ^{0}C using USP Apparatus (II) at 50 rpm. The test product should meet the following specifications:
>
> Not less than [redacted] of the labeled amount of the drug in the dosage form is dissolved in 30 minutes.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-366

Eon Labs Manufacturing, Inc.
Attention: Sadie M. Ciganek
227-15 North Conduit Avenue
Laurelton, NY 11413

JUN 10 1998

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to our "Refuse to File" letter dated May 12, 1998, and your amendment dated May 22, 1998.

NAME OF DRUG: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg

DATE OF APPLICATION: April 13, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: May 26, 1998

We will correspond with you further after we have had the opportunity to review your application.

Please identify any communications concerning this application with the number shown above.

Should you have questions concerning this application contact:

Tim Ames
Project Manager
(301) 827-5849

Sincerely yours,

Jerry Phillips
Director,
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-366

Eon Labs Manufacturing, Inc.
Attention: Sadie M. Ciganek
227-15 North Conduit Avenue
Laurelton, NY 11413

1 2 1998

Dear Madam:

Please refer to your abbreviated new drug application (ANDA) date April 13, 1998 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reason:

> You have referenced, Sotalol Hydrochloride tablets 120 mg, a strength of the reference listed drug product that has been voluntarily withdrawn from sale in the United States. Please refer to Approved Drug Products With Therapeutic Equivalence Evaluations, 18th Edition. In accord with Section 314.122 you are required to submit a citizen petition under 21 CFR 10.25(a) and 10.30 seeking a determination whether the listed drug was withdrawn for safety or effectiveness reasons.
>
> Additional supporting data is needed from the Institutional Review Board to justify the need to change the reference listed drug from 240 mg to 160 mg for *in vivo* bioequivalence testing.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(c). If you do so, the application shall be filed over protest under 21 CFR 314.101(b). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call.

Saundra T. Middleton
Project Manager
(301) 827-5862

Sincerely yours,

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

12-15 Sotalol ltr 5-7-98

April 13, 1998

Douglas L. Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: **Original ANDA**
Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg and 240 mg

Dear Mr. Sporn:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, enclosed is an original Abbreviated New Drug Application for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg and 240 mg. This application consists of the following volumes:

Volume 1	Debarment, patent and exclusivity certifications, Section 505(j)(2)(A) information, labeling, dissolution profiles, certificates of analysis, and components and composition and Raw material control data
Volume 2	Manufacturing and packaging data including executed batch records.
Volume 3	Container/closure, finished product control, methods validation, stability data, control numbers, samples, and environmental impact statement.
Volume 4 through 13	Biostudy summary and test results(Also included are the diskettes)

A full table of content precedes each appropriately paginated volume.

We have also included an analytical methods validation package in a separate volume.

In addition to the archival and review copies, we are submitting a certified true copy of the chemistry, manufacturing and controls data to the District Field Office, Brooklyn, New York. Subsequent amendments or supplements containing chemistry

manufacturing and controls data will also be submitted to the District Field Office.

If there are any comments or questions about this application, please contact me at (718) 276-8600, extension 330.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie M. Ciganek
Vice President Regulatory Affairs

Eon Labs
The Pharmacy Drug Company

227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

30, 1999

ice Fang, Ph. D.
g Director
on of Chemistry II
of Generic Drugs
r for Drug Evaluation and Research
Standish Place
Park North II
ille, MD 20857

NDA ORIG AMENDMENT

N/A 1

-TELEPHONE FACSIMILE AMENDMENT-

ence: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dr. Fang :

r the telephone conversation between Mr. Mark Anderson of FDA and Ms. Sadie Ciganek of on 4/29/99 , we are submitting this telephone facsimile amendment for Sotalol Hydrochloride ts, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA 75-366. The following are our specifications e above referenced product:

Material:

% for each unknown
% for each of the three known impurities currently identified
% total impurities

hed Product:

for any unknown individual related compound
for any known individual related compound
total related compounds

dea are the following analytical documents:

updated "**Raw Material Specification and Analysis Report**" ***(Attachment 1)***
updated Eon Labs in- house ***(Attachment 2)***
updated blank master " **Quality Control Finished Tablet Specification & Report Form**"
for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg ***(Attachment 3)***
updated ***Attachment 4)***
updated ***nt (Attachment 5)***

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MAY 0 4 1999

GENERIC DRUGS

If there are any comments or questions regarding this submission, please feel free to contact me at (718) 276-8607, extension 446.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie M. Ciganek
Vice President Regulatory Affairs

Eon Labs

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

Noted: To Maria Shih
M Anderson 3/20/00

March 15, 2000

Mr. Mark Anderson
Project Director
Food and Drug Administration
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
7500 Standish Place
Metro Park North II
Rockville, MD 20857

-- TELEPHONE AMENDMENT –

Re: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Mr. Anderson:

Reference is made to your **TELEPHONE AMENDMENT** dated March 10, 2000 commenting on our Abbreviated New Drug Application for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA # 75-366. The following are our responses to the deficiencies noted in your letter.

1. **Regarding the updated specification for Lactose, NF, it is noted that is not listed as one of the test parameters.**

   Please clarify.

   Response:

   The manufacturer of actose, has provided a letter stating that they make no claims in their product labeling regarding the content of for their lactose products. Therefore, they are not required to test for forms" based on their interpretation of the USP Pharmacopeia/NF monograph requirements. A copy of etter (which was previously submitted in the original application on page 0301) and the relevant page from USP 24 outlining the labeling requirements for actose is provided for your review, **ATTACHMENT 1**.

2. **Please provide information to demonstrate the equivalency of the new proposed liner for the 100 count.**

Response:

An illustration is included which demonstrates the equivalency of the old and new liner/ system for the 100 count. Technical data from the two are submitted, **ATTACHMENT 2.**

3. **Regarding the alternate bottle, please update page 741 of your original submission to reflect its use.**

Response:

A revision has been made to Page 0741 of our original submission including an alternate bottle, **ATTACHMENT 3**. The alternate bottle will be manufactured by using resin. Information relevant to the alternate bottle which includes a DMF referral letter and a technical data sheet is submitted,.

4. **You need to provide stability data for the 80 mg tablet in 500 count.**

Response:

We are withdrawing the 500 count for the 80 mg tablet at this time.

5. **Please provide new labeling information to reflect the addition of 500's package for the 80 mg tablet.**

Response:

Since the 500 count for the 80 mg tablet is being withdrawn, the final printed labeling submitted in our last amendment is still current. Therefore there is no need for a label change at this time.

We hope our responses satisfactorily address the deficiencies in your letter. If you have any questions, or need clarification, do not hesitate to call me at (718) 276-8600 x 315.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie M. Ciganek
Vice President Regulatory Affairs

Eon Labs

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

ORIG AMENDMENT
N/AM

February 4, 2000

Douglas L. Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

– MINOR AMENDMENT –

RE: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Mr. Sporn:

In response to your letter dated November 2, 1999 granting tentative approval for our original Abbreviated New Drug Application for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA # 75-366, we are submitting a minor amendment at least 60 days prior to the expiration of the orphan drug exclusivity, April 27, 2000 for Betapace®.

All chemistry and manufacturing controls information remain the same as currently approved with the exception of the following:

•

100 count:

If there were any further comments or questions regarding this submission, please feel free to contact me at (718) 276-8607, extension 315.

Sincerely,
Eon Labs Manufacturing, Inc.

Katrina R. Furca
Katrina R. Furca
Regulatory Affairs Associate

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

October 15, 1999

Mr. Mark Anderson
Project Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
7500 Standish Place
Metro Park North II
Rockville, MD 20857

NEW CORRESP

-TELEPHONE AMENDMENT-

Re: Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Mr. Anderson:

Reference is made to your correspondence dated October 15, 1999 commenting on the analytical method for Sotalol Hydrochloride Tablets, ANDA 75-366. Your letter states that the Philadelphia District Laboratory is having difficulty performing the assay analysis due to a large unidentified peak eluting just prior to the main peak which is causing interference with integration.

We have evaluated all relevant chromatograms for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg from the bio/ANDA batches and cannot find evidence of a peak in the area described. The chromatograms reviewed included those from the forced degradation studies and the methods validation data for assay and related substances all of which have submitted in previous amendments.These same chromatograms have been provided to the Philadelphia District Laboratory as part of the methods validation package.

We further investigated the presence of this unknown peak by evaluating recent chromatograms taken from the **Process Validation** studies that are currently in-progress in addition to examining data from the two lots of active drug substance used to make the validation batches. All chromatograms inspected were consistent with the bio/ANDA batches and did not show any evidence of an impurity eluting before the main sotalol peak. Copies of the respective chromatograms are submitted for your review:

Validation Batches

1. three (3) batches of the 80 mg
2. one (1) batch of the 120 mg
3. one (1) batch of the 160 mg
4. two (2) batches of the 240 mg

Raw Material

5. two (2) lots of API

In addition to the above chromatograms, also included is a placebo preparation chromatogram which clearly shows that there are no extra peaks caused by either the excipients or diluent.

We cannot verify the presence of this unknown peak at the District Laboratory and believe it is an anomaly which may have been introduced through external contamination during sample preparation or testing. We believe that we have demonstrated through repeated testing of our bio/ANDA batches, validation batches, and raw material lots that this peak is not in the raw material or finished product and that our validated method is acceptable for adequate peak resolution.

Please review the data submitted herein promptly so that approval of our pending ANDA is not significantly delayed. We are preparing our validation batches and anticipate a market launch immediately following the expiration of the Betapace® patent due to expire on October 29, 1999.

If you have any questions or require further information to conclude this matter, do not hesitate to call. I can be reached at (718) 276-8607 x 330.

Regards,
Eon Labs a Health Care Company

Sadie M. Ciganek
Vice President Regulatory Affairs

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

September 7, 1999

Adolph Vezza
Labeling Review Branch
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

NDA ORIG AMENDMENT

- LABELING AMENDMENT-

Re: Sotalol Hydrochloride Tablets
80 mg, 120 mg, 160 mg, and 240 mg
ANDA 75-366

Dear Mr. Vezza:

In response to your August 31, 1999 facsimile for Sotalol Hydrochloride Tablets, 80 mg, 120 mg, 160 mg, and 240 mg, ANDA 75-366, we have made the necessary revisions. Submitted herein are the final printed inserts ***(Attachment 1)***. To facilitate review of this submission, included is a side-by-side comparison of the current insert and the last submission with all differences annotated and explained ***(Attachment 2)***.

Should you require further information, please feel free to contact me at (718) 276-8600, ext. 330.

Very truly yours,
EON LABS MANUFACTURING, INC.

Sadie M. Ciganek
Vice President, Regulatory Affairs

RECD
SEP 13 1999
CDD